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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
GALVEZ, JAMES JASON	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 09/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/019,785	SAITO ET AL.	
	Examiner	Art Unit	
	J. Jason Galvez	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) *1-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/18/03, 3/26/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restriction

Applicant's election with traverse of Group I in the reply filed on 7/29/2004 is acknowledged. The traversal is on the ground(s) that an undue burden would not be placed on the Examiner because searches would be coextensive. Upon further consideration the argument that removing the restriction on the grounds that searches would not place an undue burden upon the Examiner or USPTO resources has been found persuasive. In the present application claims 1-16 are under consideration for examination.

Status of Amendments and/or Claims

The preliminary amendments of 3/26/02 and 11/26/02 have been entered in full. Claims 1-16 presented in the amendment of 3/26/02 were directed to therapeutic agents. Claims 1-16 presented as amended claims in the preliminary amendment of 11/26/02 were directed to methods, and have no resemblance to the previous claims 1-16. Therefore, the amendment of 11/26/02 was improper. However, since a restriction has already been mailed and Applicant has already elected an invention for examination the following was done to expedite prosecution. Claims 1-16 of 11/26/02 have been renumbered under 35 CFR 1.126 as claims 17-32. The claim dependencies were also corrected.

Newly submitted claims 1-16, dated on 11/26/02, are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: the original claims were directed to therapeutic agents, while the newly submitted claims were directed to methods.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 1-16, dated 3/26/02, are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Specification

The specification is objected to because it contains references to figures on page 44 ("Fig. 5") and page 62 ("Fig. 7" and "Fig. 8") that are not disclosed. The specification also contains a grammatical error on page 21, second paragraph; "Ward" should read word. Applicant is required to make proper corrections in reply to this office action.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 17-32 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 4, 6, 9-16, 19-21, and 33 of copending Application No. 09/720,326 in view of AU 199743972 B2.

Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 17-32 of the present application and claims 1, 4, 6, 9-16, 19-21, and 33 of '326 are directed towards a method of treating hypercalcemia using anti-PTHrP antibodies. There mere recitation in the present claims that the method is applicable under conditions of "drug-resistant" hypercalcemia does not make the inventions patentably distinct. With repeated use of certain drugs, such as bisphosphonates, efficacy can decrease over time, i.e. drug resistance can occur [AU 199743972 B2, p.4 lines 19-23]. The two inventions have overlapping patient populations and are consequently directed towards the same invention. Furthermore, the specific limitations recited in the claims of '326 are species, which render the genus of "substances" and conditions recited in the instant claims obvious.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The factors to be considered have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breath of claims. *Ex Parte Forman*, (230 USPQ 546 (Bd. Pat. App. & Int. 1986)); *In re Wands*, 858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988).

Claims 17-32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating bisphosphonate-resistant and calcitonin-resistant hypercalcemia using humanized antibody 23-57-137-1, does not reasonably provide enablement for treating or preventing drug-resistant hypercalcemia in general using an undetermined and unspecified antagonist of PTHrP receptors and anti-PTHrP antibodies. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or the invention commensurate in scope with these claims.

Claim 17 and all of the dependent claims, 18-32, are drawn to "preventing or treating at least one symptom of drug-resistant hypercalcemia". By definition (Merriam-Webster Online Dictionary) prevent means to "3: to keep from happening or existing", which the Applicant has not shown. For example, figure 2 illustrates that administration of antibody was able to partially restore, i.e. treat, body weight, however this illustration along with the other illustrations fail to meet the requirement for "preventing" at least one symptom of drug-resistant hypercalcemia. In addition, "at least one symptom" could encompass a myriad of symptoms ranging from soft tissue calcification to seizures to death, however the present disclosure only talks about two symptoms of hypercalcemia: blood calcium quantities and body weight. It is unclear whether or not the present invention would have therapeutic use geared towards other symptoms of hypercalcemia. Therefore, it would be impossible to make and/or use the invention commensurate in scope due to the quantity of experimentation necessary, the nature of the invention, the state of the prior art, the unpredictability of the art, and the breath of the claims.

Claims 17-18 and all of the dependent claims, 19-32, are drawn to "at least one substance that inhibits the binding between PTHrP and a receptor thereof", which can encompass potentially thousands upon thousands of compounds including different antibodies, different polypeptides occurring in nature and through synthetic processes, and natural or synthetic inorganic compounds to name a few. Therefore, it would be impossible to make and/or use the invention commensurate in scope due to the quantity of experimentation

necessary, the absence of adequate working examples, the nature of the invention, the relative skill of those in the art, the unpredictability of the art, and the breadth of the claims.

Claim 18 and all of the dependent claims, 19-32, are drawn to "wherein the drug-resistant hypercalcemia is resistant to a therapeutic agent for hypercalcemia". The only therapeutic agents disclosed is a bisphosphonate (Alendronate) and a calcitonin (Elcatonin), which fails to take into consideration the other potential therapeutic agents that may exhibit drug-resistant hypercalcemia making it impossible to know if the present invention could be used in the broad sense claimed. It is even conceivable that the present invention may at some point show drug-resistant hypercalcemia. Therefore it would be impossible to make and/or use the invention commensurate in scope due to the quantity of experimentation necessary, the absence of an adequate number of working examples, and the breadth of the claims.

Claim 19 is drawn to "bone resorption-inhibiting agent, a calcium excretion-promoting agent, an agent for inhibiting intestinal absorption of calcium, and a loop diuretic". The only agents or compounds disclosed are a bisphosphonate (Alendronate) and a calcitonin (Elcatonin). The Applicant has supplied no support for the breadth of the claim in regards to the class of compounds recited "a calcium excretion-promoting agent, an agent for inhibiting intestinal absorption of calcium, and a loop diuretic". Therefore it would be impossible to make and/or use the invention commensurate in scope due to the

quantity of experimentation necessary, the absence of an adequate number of working examples, and the breadth of the claims.

Claim 20 is drawn to "a bone resorption-inhibiting agent". The only bone resorption-inhibiting agents disclosed are a bisphosphonate (Alendronate) and a calcitonin (Elcatonin). The Applicant has failed to disclose the use of the present invention with respect to this class of drugs (bone resportion-inhibiting agents) making it unknown if the present invention can be used under conditions of drug-resistant hypercalcemia where the drug-resistant hypercalcemia is resistant to the number of other compounds classified as bone-resportion inhibiting agents. Therefore it would be impossible to make and/or use the invention commensurate in scope due to the quantity of experimentation necessary, the absence of an adequate number of working examples, and the breadth of the claims.

Claim 21 is drawn to "at least one of bisphosphonate and calcitonin", which does not limit the claim to bisphosphonate or calcitonin. As presented the claim is limited to a bone resportion-inhibiting agent. The only bone resorption-inhibiting agents disclosed are a bisphosphonate (Alendronate) and a calcitonin (Elcatonin). The Applicant has failed to disclose the use of the present invention with respect to this class of drugs (bone resportion-inhibiting agents) making it unknown if the present invention can be used under conditions of drug-resistant hypercalcemia where the drug-resistant hypercalcemia is resistant to the number of other compounds classified as bone-resportion inhibiting agents. Therefore it would be impossible to make and/or use the invention commensurate in scope

due to the quantity of experimentation necessary, the absence of an adequate number of working examples, and the breadth of the claims.

Claims 22 and 30 are drawn to "an antagonist of the PTHrP receptor" and do not specify the antagonist. The Examiner has interpreted this to mean any PTHrP receptor antagonist. The specification fails to disclose the vast number of PTHrP receptor antagonist that may or may have the ability to operate within the framework of the present invention. Therefore it would be impossible to make and/or use the present invention commensurate in scope due to the quantity of experimentation necessary, the lack of direction or guidance, the absence of adequate working examples, and the breadth of the claims.

Claims 23-27 and 30-31 are drawn to "anti-PTHrP antibody" or "antibody". The Examiner has interpreted this to mean any antibody raised against PTHrP. The specification fails to disclose the vast number of anti-PTHrP antibodies that can be directed towards different regions of PTHrP, which may or may have the ability to operate within the framework of the present invention. Therefore it would be impossible to make and/or use the present invention commensurate in scope due to the quantity of experimentation necessary, the lack of direction or guidance, the absence of adequate working examples, the unpredictability of the art, and the breadth of the claims.

Claims 17-18, 20 and 22-24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the

inventor(s), at the time the application was filed, had possession of the claimed invention.

The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, and any combination thereof.

Claims 17-18 are drawn to "at least one substance that inhibits the binding between PTHrP and a receptor thereof" and do not meet written description requirements. The "at least one substance" in the present invention could theoretically be a myriad of chemicals, biological molecules, and/or compounds. Therefore, a person of ordinary skill in the art cannot envision the methods of the present invention because the only disclosure of such substances that can inhibit the binding of PTHrP and its receptor is an anti-PTHrP antibody. Accordingly, the specification does not provide adequate written description of the claimed genus of substances that inhibit the binding between PTHrP and it receptor.

Claim 20 is drawn to "bone resorption-inhibiting agent" and does not meet written description requirements. Bone resorption-inhibiting agents comprise a broad class of drugs that could have effects on osteoclast (bone degradation) and/or osteoblast (bone formation) activity. Therefore, a person of ordinary skill in the art cannot envision the methods of the present invention due to the great number of drugs that are being claimed as an essential part of the invention, i.e. the type of drug-resistant hypercalcemia. The only adequately described species of bone-resoption inhibiting agents is a single bisphosphonate and a single

calcitonin. Accordingly, the specification does not provide adequate written description of the claimed genus of bone-resorption inhibiting agents.

Claim 22 is drawn to "an antagonist of the PTHrP receptor" and does not meet written description requirements. Antagonists can range from ligand binding to receptor binding. Additionally, there are at least four different kinds of receptor antagonists: competitive, non-competitive, partial agonists, partial antagonists. The only adequately described species of antagonists is an antibody that is directed to the ligand. Accordingly, the specification does not provide adequate written description of the claimed genus of antagonists.

Claims 23 and 24 are drawn to "an anti-PTHrP antibody" and "a fragment of an anti-PTHrP antibody", respectively, and do not meet written description requirements. Antibodies can be directed towards different epitopes or antigenic determinant sites. The only adequately described species of antibody or antibody fragments is one antibody, designated #23-57-137-1. Accordingly, the specification does not provide adequate written description of the claimed genus of antibody or antibody fragments.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 17-32 are rejected under 35 U.S.C. 102(b) as being anticipated by Sato et al. [AU 199743972 B2 (04/17/98)]. Sato et al. teach that PTHrP is involved in hypercalcemia associated with malignancy and that repeated treatment using calcitonin, bisphosphonate, etc. results in decreased efficacy, i.e. drug-resistant hypercalcemia, over time (p. 4 lines 14-23). Sato et al. also teach that since drug-resistance occurs as a result of repeated exposure to certain compounds a novel approach may be to use antibodies directed towards PTHrP (p. 4 lines 24-28/p. 5 lines 1-19). In particular, humanized antibodies with the designation 23-57-137-1 are used in examples present in Figure 12. Thus, Sato et al. meet the limitations of all of the claims in the instant application.

Conclusion

NO CLAIM IS ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **J. Jason Galvez, Ph.D**. whose telephone number is **571-272-2935**. The examiner can normally be reached Monday through Friday 9 AM to 5 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Brenda Brumback, Ph.D.** can be reached at **571-272-0887**.

The fax phone number for the organization where this application or proceeding is assigned is **703-872-9306**. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained

from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER

JJG
9/13/04